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(54) **LIQUID DISPENSING ASSEMBLY FRAME**

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G01N 21/00	(2006.01)
G01N 21/47	(2006.01)
B41J 2/135	(2006.01)
B01L 3/02	(2006.01)
B41J 2/045	(2006.01)
G01N 21/51	(2006.01)
B41J 2/21	(2006.01)
G01N 35/10	(2006.01)

(52) **U.S. Cl.**

CPC ***B01L 3/0268*** (2013.01); ***B41J 2/04561*** (2013.01); ***G01N 21/51*** (2013.01); *B01L 2200/061* (2013.01); *B01L 2200/0642* (2013.01); *B01L 2200/143* (2013.01); *B01L 2400/02* (2013.01); *B41J 2/0451* (2013.01); *B41J 2/2142* (2013.01); *G01N 35/1016* (2013.01); *G01N 2021/513* (2013.01); *Y10T 436/25* (2015.01)

(58) **Field of Classification Search**

CPC .. B41J 2/14024; B41J 2/175; B41J 2/04561; B41J 2/1752; B41J 2/14072

See application file for complete search history.

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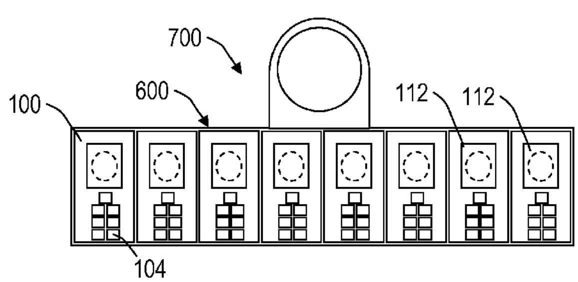
(57) **ABSTRACT**

Various techniques for dispensing liquids are disclosed herein. In one embodiment a dispenser retention apparatus includes a frame. The frame includes a top surface configured to retain a liquid dispensing assembly. The frame also includes a bottom surface opposite the top surface. The bottom surface includes a first channel extending from a first lateral edge of the frame to a droplet passage between the top and bottom surfaces. The first channel is configured to allow a light beam introduced to the frame at the first lateral edge to intersect a droplet in the passage.

17 Claims, 7 Drawing Sheets



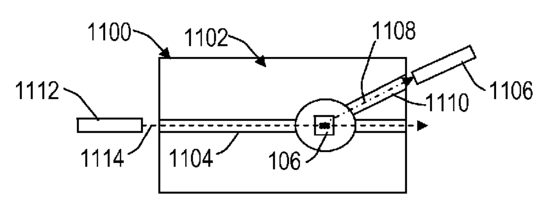


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Fig. 1

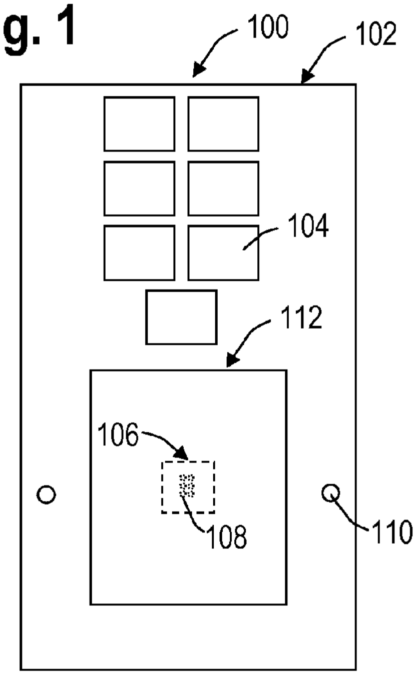


Fig. 2

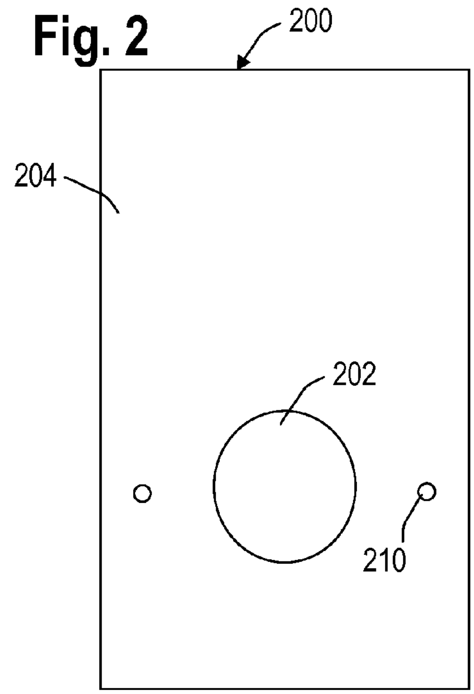


Fig. 3A

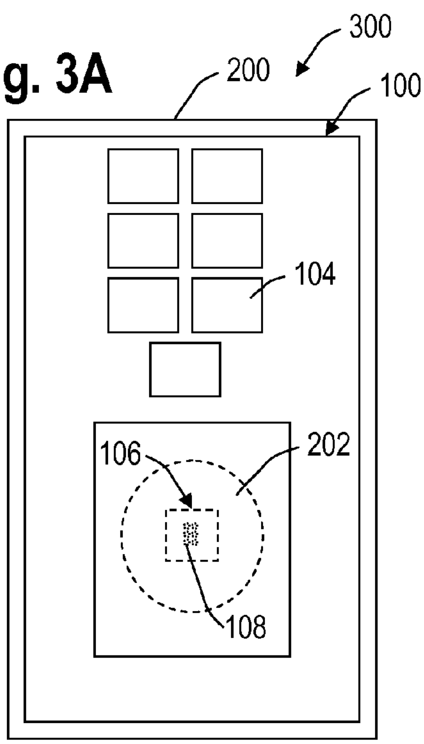
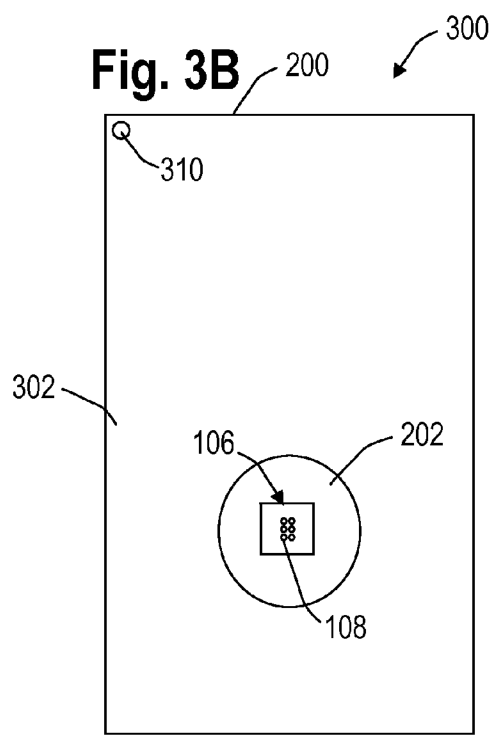


Fig. 3B



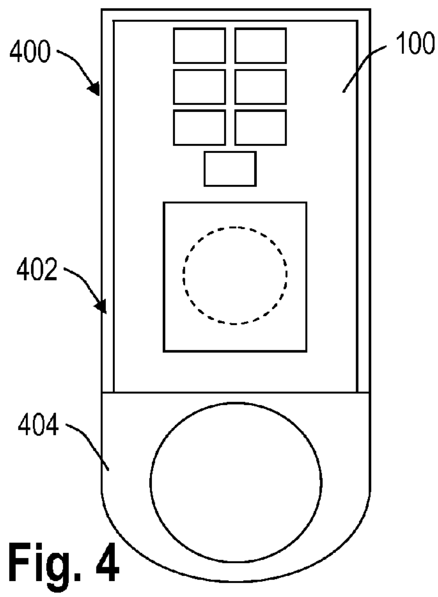


Fig. 4

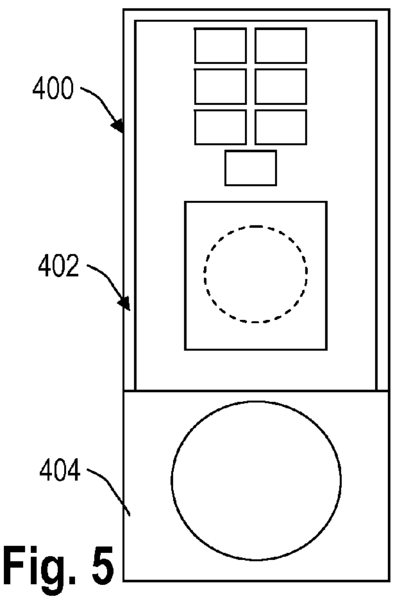


Fig. 5

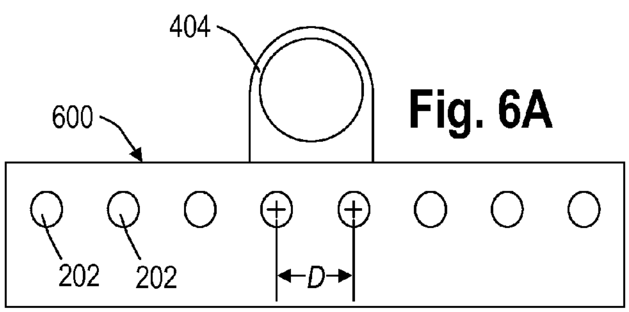


Fig. 6A

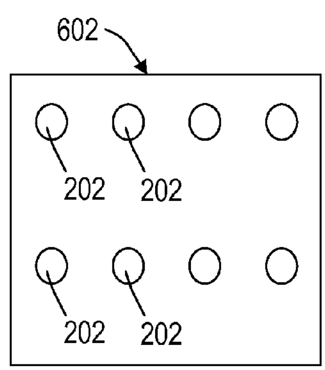


Fig. 6B

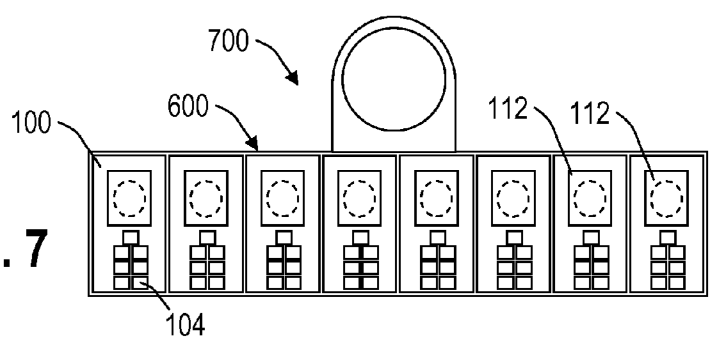


Fig. 7

Fig. 8

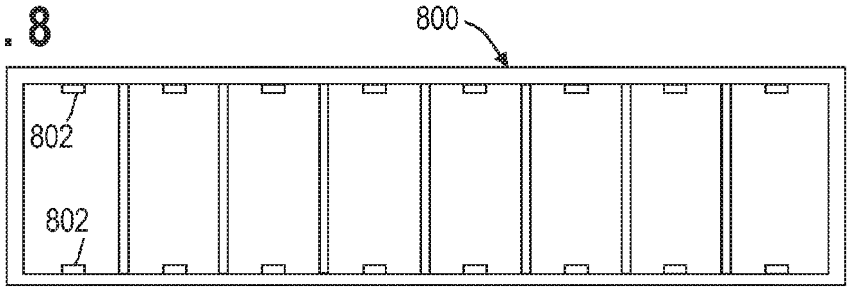


Fig. 9A

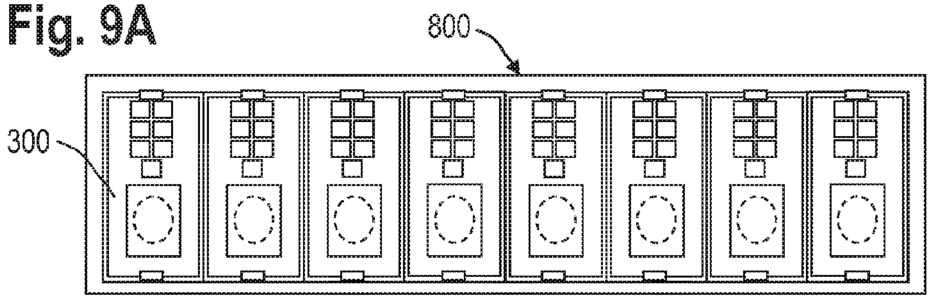
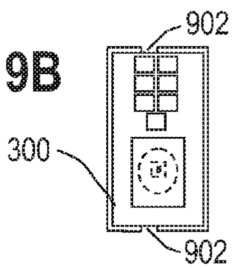


Fig. 9B



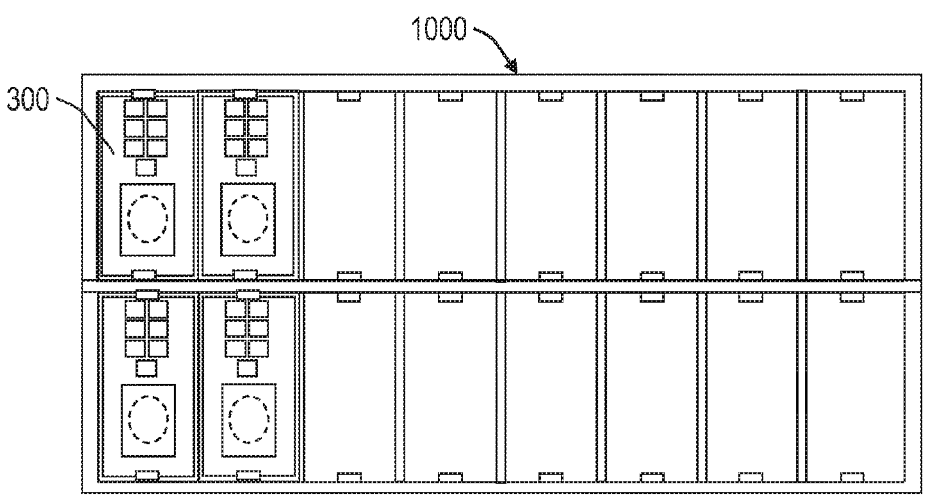


Fig. 10

Fig. 11

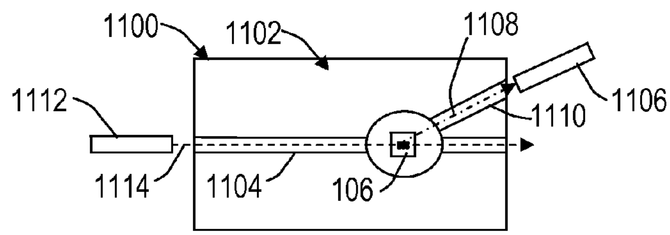


Fig. 12

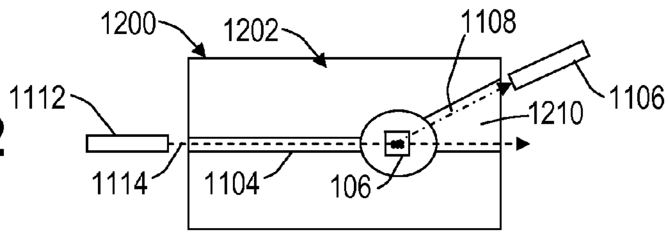


Fig. 13

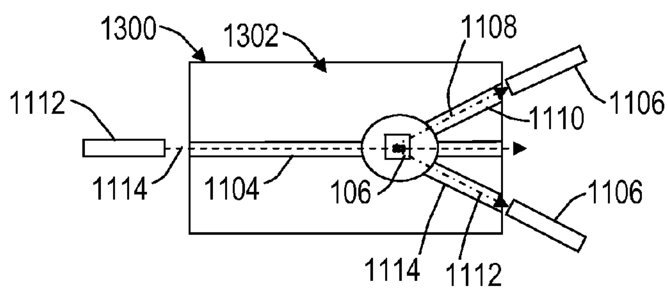


Fig. 14

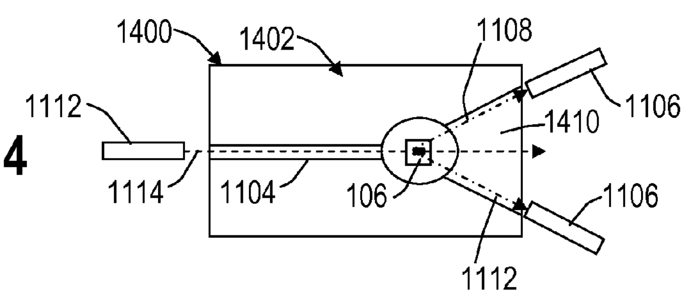


Fig. 15

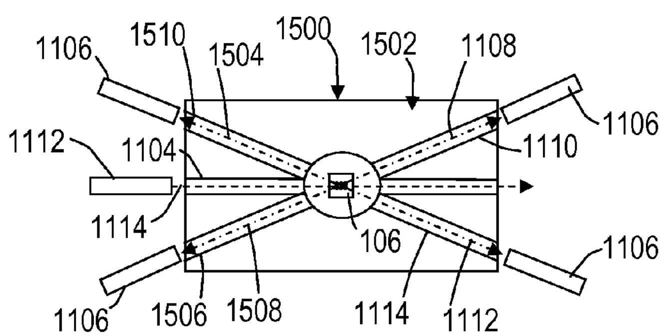


Fig. 16

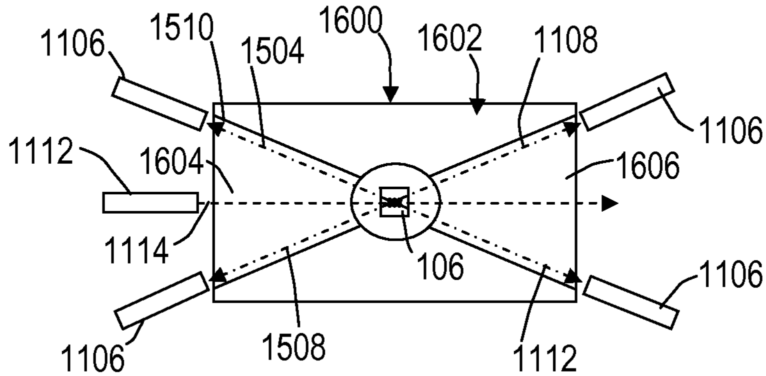


Fig. 17

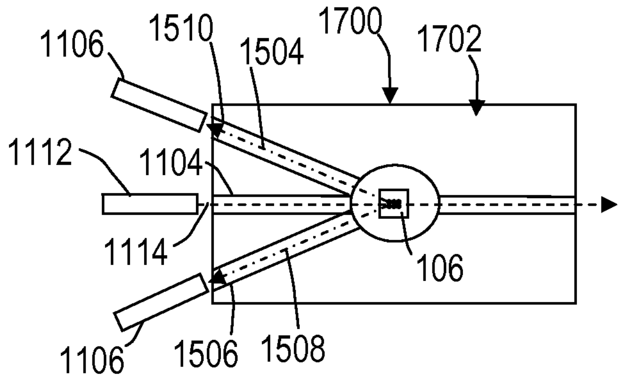
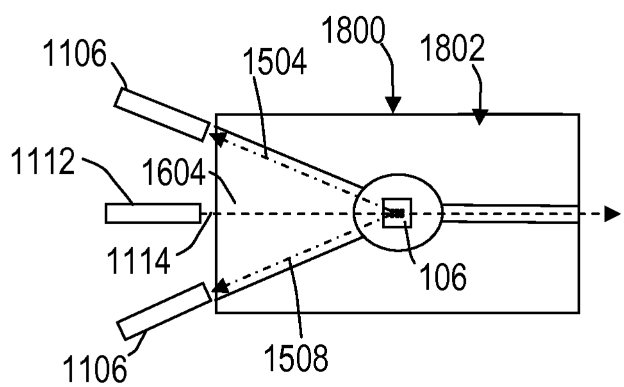


Fig. 18



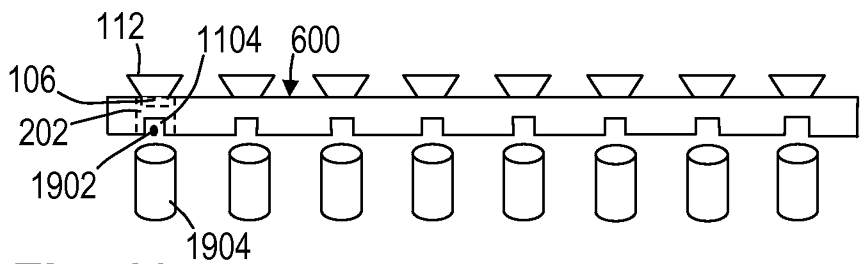

112
1104
600
106
202
1902
1904

Fig. 19

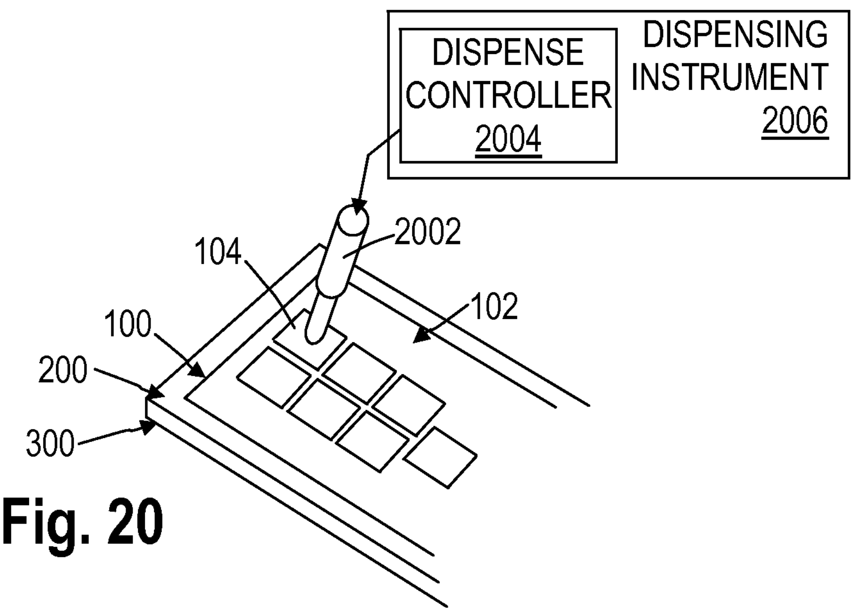
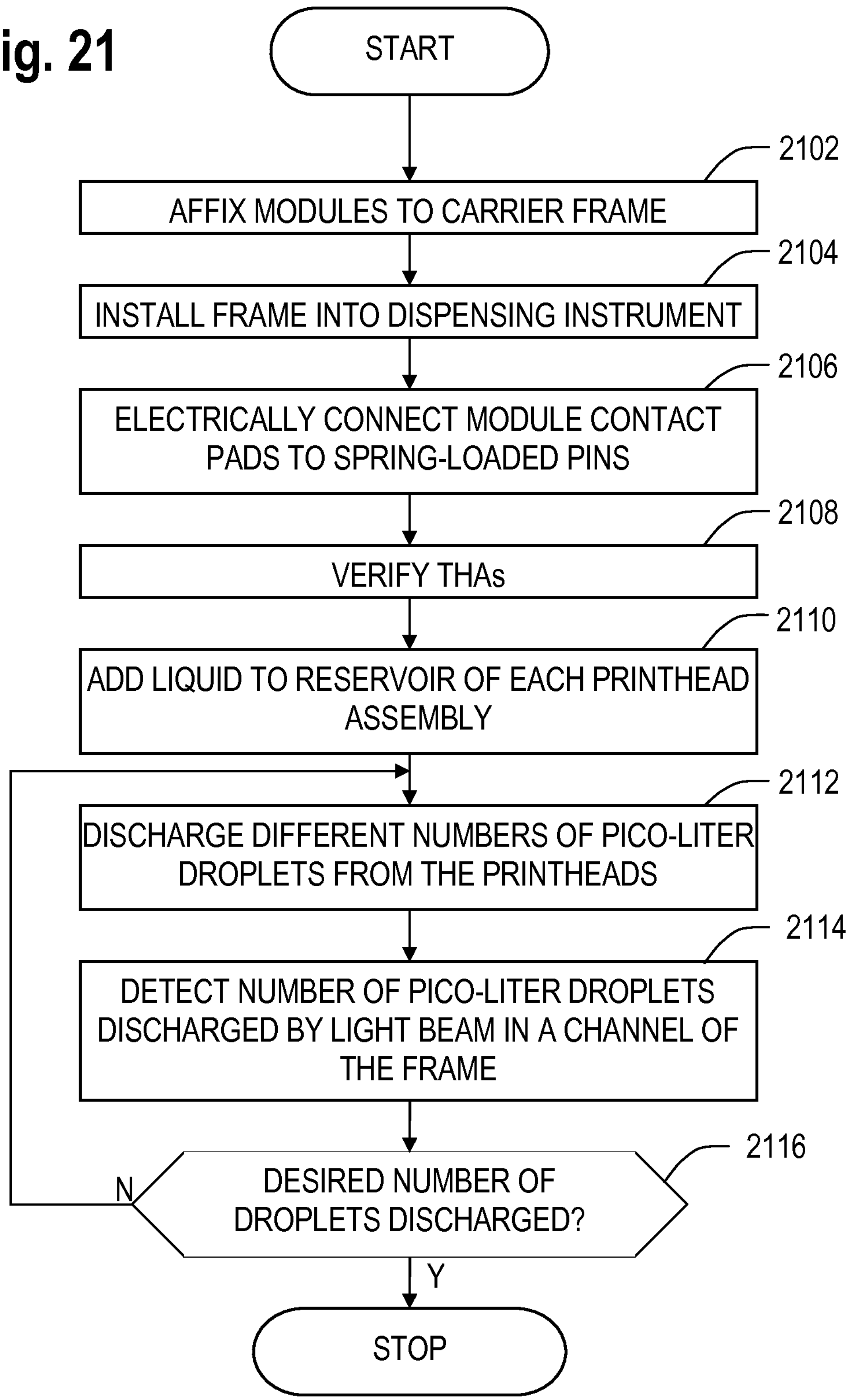

DISPENSE
CONTROLLER
2004
DISPENSING
INSTRUMENT
2006
2002
104
102
100
200
300

Fig. 20

Fig. 21


START
2102
AFFIX MODULES TO CARRIER FRAME
2104
INSTALL FRAME INTO DISPENSING INSTRUMENT
2106
ELECTRICALLY CONNECT MODULE CONTACT PADS TO SPRING-LOADED PINS
2108
VERIFY THAs
2110
ADD LIQUID TO RESERVOIR OF EACH PRINTHEAD ASSEMBLY
2112
DISCHARGE DIFFERENT NUMBERS OF PICO-LITER DROPLETS FROM THE PRINTHEADS
2114
DETECT NUMBER OF PICO-LITER DROPLETS DISCHARGED BY LIGHT BEAM IN A CHANNEL OF THE FRAME
2116
DESIRED NUMBER OF DROPLETS DISCHARGED?
N
Y
STOP

LIQUID DISPENSING ASSEMBLY FRAME

BACKGROUND

Dispensing of liquids in volumes from picoliters to microliters is an essential operation in many areas of pharmaceutical and biology research, as well as in medical and veterinary diagnostics, forensics testing, and agricultural testing. Even within these fields, low-volume liquid dispensing is used for many different operations.

One stage of pharmaceutical research, during which low-volume liquid dispensing is important, is directed to determining the concentration of a compound needed to effectively attack or inhibit a target (e.g., a virus). Many different concentrations of the compound are created in containers, such as the wells of a microplate (also known as a "well plate") to determine the effective concentration. Dispensing systems direct liquids into the wells. Serial dilution is applied to achieve a required concentration when the dispensing system is incapable of providing sufficiently small volumes of the compound.

BRIEF DESCRIPTION OF THE DRAWINGS

For a detailed description of exemplary embodiments of the invention, reference will now be made to the accompanying drawings in which:

FIG. **1** shows a top view of a head assembly in accordance with various embodiments;

FIG. **2** shows a top view of a frame configured to support a head assembly in accordance with various embodiments; and

FIGS. **3**A and **3**B show top and bottom views of a head assembly module in accordance with various embodiments;

FIGS. **4** and **5** show a top view of a head assembly module including a handling feature in accordance with various embodiments;

FIGS. **6**A and **6**B show a top views of frames configured to support one and two-dimensional arrays of head assemblies in accordance with various embodiments;

FIG. **7** shows a top view of a head assembly module including a one-dimensional array of head assemblies in accordance with various embodiments;

FIG. **8** shows a top view of a frame configured for user insertion of head assemblies in a one dimensional array in accordance with various embodiments;

FIG. **9**A shows a top view of a fully populated frame configured for user insertion of a head assemblies in a one dimensional array in accordance with various embodiments;

FIG. **9**B shows a top view of a head assembly module that includes alignment/retention features in accordance with various embodiments;

FIG. **10** shows a top view of a partially populated frame configured for user insertion of head assemblies in a two dimensional array in accordance with various embodiments;

FIGS. **11**-**18** show a bottom view of a frame including channels for light scattering drop detection in accordance with various embodiments;

FIG. **19** shows a side view of a populated frame in accordance with various embodiments;

FIG. **20** shows a top view of a head assembly module with spring loaded pin connection in accordance with various embodiments; and

FIG. **21** shows a flow diagram for a method of titration in accordance with various embodiments.

NOTATION AND NOMENCLATURE

Certain terms are used throughout the following description and claims to refer to particular system components. As one skilled in the art will appreciate, computer companies may refer to a component by different names. This document does not intend to distinguish between components that differ in name but not function. In the following discussion and in the claims, the terms "including" and "comprising" are used in an open-ended fashion, and thus should be interpreted to mean "including, but not limited to . . . . " Also, the term "couple" or "couples" is intended to mean either an indirect, direct, optical or wireless electrical connection. Thus, if a first device couples to a second device, that connection may be through a direct electrical connection, through an indirect electrical connection via other devices and connections, through an optical electrical connection, or through a wireless electrical connection.

DETAILED DESCRIPTION

The following discussion is directed to various embodiments of the invention. Although one or more of these embodiments may be preferred, the embodiments disclosed should not be interpreted, or otherwise used, as limiting the scope of the disclosure, including the claims. In addition, one skilled in the art will understand that the following description has broad application, and the discussion of any embodiment is meant only to be exemplary of that embodiment, and not intended to intimate that the scope of the disclosure, including the claims, is limited to that embodiment.

One stage of pharmaceutical research is directed to determining the concentration of a compound needed to effectively attack a target (e.g., a virus). To determine an effective concentration of a compound, many different concentrations of the compound are created in trays of miniature test tubes called "well plates." A dispensing system distributes the compound into the well. If the dispensing system is unable to dispense sufficiently small volumes of the compound, serial dilution is applied to achieve a desired concentration.

Disclosed herein are techniques for using a frame conveying one or more liquid dispensing assemblies (e.g., titration head assemblies ("THA")) to dispense small volumes (e.g., pico-liters) of liquid very quickly. Such techniques provide a method to titrate solutions across many orders of magnitude of concentration without serial dilution. Those same techniques can be used to dispense low-volumes of a wide-variety of liquids containing active biological ingredients, assay components, markers, tags, or a wide variety of other fluids relevant to the fields of pharmaceutical research, bio research, forensics study, veterinary research and diagnostics, and medical diagnostics, to name a few. Embodiments of the frame may include one or two-dimensional arrays of THAs spaced in accordance with the wells of a microplate. Frame embodiments can also include multiple THA designs for dispensing a variety of fluids into many bioassay and other applications requiring similar technology.

Embodiments of the frame also include channels formed in the bottom surface of the frame. The channels improve the accuracy of light scattering drop detection by reducing the distance between dispenser nozzles a light beam passing below the nozzles, thereby permitting laser light to pass through and not be reflected, and enabling use of a higher numerical aperture fiber.

In some embodiments, THAs are rigidly attached to a frame with a solid bottom surface, and/or the frame includes features for ease and stability of stacking the frames, and/or the frame includes numbers for each THA or other human or machine readable ID marks on the frames to denote each THA or features of the frame or THAs.

FIG. **1** shows a top view of a THA **100** in accordance with various embodiments. The THA **100** includes a flexible substrate **102** (e.g., polyimide), electrical contact pads **104**, a liquid reservoir **112**, and a printhead **106** including an array of nozzles **108**. The THA **100** may also include an alignment mark, for example, fiducials **110** for aligning the THA on a frame. The THA also includes conductive traces between the pads **104** and the printhead **106**.

The printhead **106** may be based on, for example, thermal inkjet technology, or any other liquid dispensing technology capable of producing a desired droplet size. Embodiments of the printhead **106** may differ as to the number of nozzles **108**, distribution of the nozzles **108**, the type of fluid accommodated by the printhead **106** fluid chamber (e.g., aqueous, dimethyl sulfoxide, etc.), droplet volume, etc. With regard to droplet volume for example, one embodiment of the printhead **106** discharges **1**-pico-liter droplets, another embodiment discharges **10**-pico-liter droplets, and yet another embodiment discharges **100**-pico-liter droplets. Similarly, embodiments of the THA **100** may include different liquid reservoirs **112** capable of holding different volumes of liquid (e.g., a 5 micro-liter reservoirs **112**, a 50 micro-liter reservoirs receptacles **112**, etc).

FIG. **2** shows a top view of frame **200** configured to support a titration head assembly **100** in accordance with various embodiments. The upper surface of the frame **200** is non-conductive in some embodiments to allow the titration head assembly **100** to be bonded to the frame **200** without shorting conductors of the THA **100**. The frame **200** may be formed of a polymer material or may be metal or ceramic. A metallic frame may include a non-conductive coating in some areas to prevent the conductors of the THA **100** from shorting. An opening **202** is disposed in the frame **200** to allow droplets produced by the printhead **106** to pass through the frame **200**. The frame **200** may also include alignment features **210** that guide placement of the THA **100** on the frame **100**. The frame **200** is rigid enough to maintain its shape when electrical connections are made with the pads **104** via spring-loaded pins or another electrical connection method.

FIG. **3**A shows a top view of a THA module **300** in accordance with various embodiments. The THA module **300** includes a THA **100** mounted onto a frame **200**. The THA **100** may be bonded to the frame **200** by an adhesive. The THA **100** is aligned and secured to the frame **200** such that the nozzles **108** face into the opening **202** of the frame **200**. The frame **200** provides support for the electrical contact pads **104** allowing electrical connections to be made with the pads **104** via spring-loaded pins when the frame is positioned in a dispensing instrument. The bottom surface **302** of the frame **300** may extend no more than 2 millimeters ("mm") (e.g., 0.50-2 mm in some embodiments) below the printhead **106**, in some embodiments, to provide small printhead to drop receptacle spacing.

The frame **200** provides a reference for positioning the THA **100** for use. For example, by positioning the frame **200** relative to a receptacle intended to receive liquid from the THA **100**, and/or a liquid delivery system configured to load the reservoir **112**, the reservoir **112**, printhead **106**, pads **104**, etc. are positioned for proper operation. By affixing the THA **100** to the rigid frame **200**, the orientation of the THA **100** (e.g., horizontality of the printhead **106** and/or reservoir **112**) can be controlled by controlling the orientation of the frame **200**.

FIG. **3**B shows a bottom view of the THA module **300** in accordance with various embodiments. The THA module **300** may include alignment features **310** allowing the module **300** to be properly positioned in a dispensing instrument and/or relative to a container positioned to receive liquid from the module **300**. In some embodiments, the module **300** may be 9 mm or less in width and/or 25 mm or less in length. In some embodiments, the module **300** may be 4.5 mm or less in width.

FIGS. **4** and **5** show a top view of a THA module **400** in accordance with various embodiments. The module **400** includes a THA **100** affixed to a frame **402**. The frame **402** is similar to the frame **200**, and further includes a handling feature **404** (i.e., a grip area) to facilitate handling by a user.

FIG. **6**A shows a top view of a frame **600** configured to support a one-dimensional array of THAs **100** in accordance with various embodiments. The frame **600** is configured to support up to eight THAs **100**. Other embodiments may be configured to support more or fewer THAs **100**. For example, an embodiment of the frame may be configured to support up to 16 THAs **100**. The frame **600** includes a handling feature **404**. Some embodiments may omit the handling feature **404**. The openings **202** may be spaced to in accordance with a desired droplet receptacle spacing. For example, in some embodiments the openings **202** may be spaced by an integer multiple of 2.25 mm to align with industry standard microplate well spacing. Some embodiments of the frame **600** are dimensioned (e.g., 1"×3") to allow manipulation by microscope slide robotics. Some embodiments of the frame **600** are dimensioned (e.g.; 3.5"×5") to allow manipulation by microplate handling grippers and storage in microplate stacks and shelves.

FIG. **6**B shows a top view of a frame **602** configured to support a two-dimensional array of THAs **100** in accordance with various embodiments. The frame **602** is configured to support up to eight THAs **100**. Other embodiments may be configured to support more (e.g., 16) or fewer THAs **100**, by providing for a different number of rows and/or columns of THAs **100**. The openings **202** may be spaced to in accordance with a desired droplet receptacle spacing (e.g., microplate well spacing, D=2.25 mm, D=4.5 mm, D=9 mm, etc). The frame **602** may be dimensioned to allow manipulation by microplate handling grippers and storage in microplate stacks and shelves.

FIG. **7** shows a top view of a head assembly module **700** including a one-dimensional array of THAs **100** affixed to the frame **600** in accordance with various embodiments. Different liquids and/or different volumes of liquid may be loaded into different ones of the receptacles **112**, and the THAs **100** of the module **700** may be dispensed from serially or in parallel to reduce microplate processing time. Electrical connections can be made to the electrical contact pads **104** one THA **100** at a time or to many or all THAs **100** simultaneously.

FIG. **8** shows a top view of a carrier frame **800** configured for user insert on of head assembly modules **300** (or other one-dimensional modules, e.g., 1×2, 1×4, etc.) in a one-dimensional array in accordance with various embodiments. The carrier frame **800** allows for provision of a user selectable number of THA modules **300** to a dispensing instrument. The THAs **100** may snap into the carrier frame **800** using an alignment/retention feature **802** of the carrier frame **800** that cooperatively engages an associated feature of the module **300**. The carrier frame **800** may be configured for handling by microscope slide robotics. Some embodiments of the carrier frame **800** are dimensioned to allow manipulation by microplate handling grippers and storage in microplate stacks and shelves. Some embodiments of the carrier frame **800** space the THA modules **300** in accordance with a desired drop receptacle spacing (e.g., an industry standard spacing, such as 9 mm, 4.5 mm, or 2.25 mm, or an integer multiple thereof).

FIG. **9**A shows a top view of the carrier frame **800** fully populated with THA modules **300** in accordance with various embodiments. FIG. **9**B shows a top vie of a THA module **300** that includes alignment/retention features **902**. In some embodiments, friction between the alignment/retention features **802**, **902** retains the THA module **300** in the carrier frame **800**. In some embodiments, the carrier frame **800** extends no more than 2 millimeters below the printhead **106** to provide small printhead to drop receptacle spacing.

FIG. **10** shows a top view of a partially populated carrier frame **1000** configured for user insertion of THA modules **300** (or other one or two-dimensional THA modules) in a two dimensional array in accordance with various embodiments. The carrier frame **1000** is configured to support up to 16 THA modules **300**. A user may mount as many THA modules **300** as desired in the carrier frame **1000** at a time selected by the user (e.g., at time of use). Other embodiments of the carrier frame **1000** support more or fewer rows and/or columns of THA modules. The carrier frame **1000** may be configured for automated handling by microplate idling robotics.

FIGS. **11**-**15** show a bottom view of a THA module **300** including channels for light scattering drop detection ("LSDD") in accordance with various embodiments. Light scattering drop detection uses light scattered by a droplet passing through a light beam to detect the presence of the droplet. Performance of LSDD may be compromised when a THA **100** is mounted on a frame because the frame thickness increases the distance between the light beam and the surface of the printhead **106**. To improve LSDD performance, embodiments of the frame **200**, **400**, **600**, **800**, **1000** include channels formed in the bottom side of the frame to reduce the distance between the light beam and the surface of the printhead **106**. Channels also let the light beam pass through the frame without being reflected into a light collector. The channels also enable use of a higher numerical aperture light collector which allows for detection of more scattered light. Channel depth may range, for example, from 0.1 mm to 1.9 mm for a 2 mm frame (i.e., thickness of frame material above a channel may range from about 0.1 mm to about the frame thickness less 0.1 mm). A thicker frame may have a deeper channel in order to reduce spacing between the light beam and the surface of the printhead **106**.

FIG. **11** shows a THA module **1100** including a frame **1102**. The frame **1102** is similar to the frame **200** and includes channels (grooves) **1104** and **1110** provided in the bottom of the frame **1102**. The channel **1104** allows light beam **1114** provided by light source **1112** to pass between the bottom surface of the frame **200** and the printhead **106**, thereby reducing the distance between the beam **1114** and the printhead **106**. As a droplet is discharged from the printhead **106** the beam **1114** intersects the droplet, and the droplet scatters the light beam **1114**. Scattered light **1108** is collected by light collector **1106** via a channel **1108** formed in the bottom of the frame **200**. In some embodiments, the light source **1112** is a laser light source (e.g., a laser diode), and the light collector **1106** is an optical fiber. The light collector **1106** provides light to a processing system that analyzes the collected light to identify droplets. Embodiments provide the channel **1110** at an angle of 15 degrees plus or minus 10 degrees from the channel **1104**.

FIG. **12** shows a THA module **1200** including a frame **1202**. The frame **1202** is similar to the frame **1102**, but includes a triangular channel **1210** for collection of scattered light **1108**. In some embodiments, the channel **1210** occupies an area extending from 0 degrees to 25 degrees from the channel **1104**.

FIG. **13** shows a THA module **1300** including a frame **1302**. The frame **1302** is similar to the frame **1102**, but includes an additional channel **1114** for passage of scattered light **1112** for collection by a second instance of the light collector **1106**. Embodiments provide the channel **1114** at an angle of 15 degrees plus or minus 10 degrees from the channel **1104**.

FIG. **14** shows a THA module **1400** including a frame **1402**. The frame **1402** is similar to the frame **1202**, but includes an enlarged triangular channel **1410**. The channel **1410** provides passage for reception of scattered light **1108** and **1112** by light detectors. The channel **1410** allows capture of detected light at up to approximately a 25 degree angle from the light beam **1114**.

FIG. **15** shows a THA module **1500** including a frame **1502**. The frame **1502** is similar to the frame **1302**, but includes additional channels **1506** and **1510** for passage of back-scattered light **1508**, **1504** for collection by light collectors **1106**. Embodiments provide the channels **1506**, **1510** at an angle of 15 degrees plus or minus 10 degrees from the channel **1104**.

FIG. **16** shows a THA module **1600** including a frame **1602**. The frame **1602** is similar to the frame **1502**, but includes enlarged triangular channels **1604**, **1606**.

FIG. **17** shows a THA module **1700** including a frame **1702**. The frame **1702** is similar to the frame **1502**, but omits the channels **1110** and **1114**. Thus, the frame **1702** is configured for collection of back-scattered light **1504**, **1508**.

FIG. **18** shows a THA module **1800** including a frame **1802**. The frame **1802** is similar to the frame **1702**, but includes an enlarged triangular channel **1604**. Thus, the frame **1802** is configured for collection of back-scattered light **1504**, **1508**.

FIG. **19** shows a side view of a frame (e.g., frame **600** or frame **800**) populated with THAs **100** in accordance with various embodiments. The printhead **106** is positioned in the opening **202** in the frame **600**. Liquid is provided from the reservoir **112** to the printhead **106**. The printhead **106** is activated to expel a droplet **1902** (e.g., a pico-liter droplet) that descends through the opening **202** in the frame **600** into a container **1904** located below the frame **600**. The container **1604** may be a well of a microplate.

FIG. **20** shows a top view of a THA module **300** with spring-loaded pin connection in accordance with various embodiments. The frame **200** provides support for the contact pads **104** allowing the spring-loaded pin **2002** to make an electrical connection with the pad **104** without deforming the flexible substrate **102** of the THA **100**. Only a single spring-loaded pin **2002** is shown for purposes of illustration. In practice however, a spring-loaded pin **2002** may be provided for as many of the pads **104** as needed to provide power and control signals to the print head **106** from the dispense controller **2004** of a dispensing instrument **2006** with which the module **300** is used. Furthermore, spring-loaded pins **2002** may be provided for as many THAs **100** as are mounted on a module **700** and/or a user configurable carrier frame **800**, **1000**.

FIG. **21** shows a flow diagram for a method of titration in accordance with various embodiments. Though depicted sequentially as a matter of convenience, at least some of the actions shown can be performed in a different order and/or performed in parallel. Additionally, some embodiments may perform only some of the actions shown. At least some of the actions shown may be performed by logic of a dispensing instrument **2006**. In some embodiments, such logic may include a processor executing software instructions stored in a computer readable medium.

In block **2102**, a user affixes THA modules (e.g., THA module **300**) to a carrier frame (e.g., carrier frame **800**). The carrier frame **800** may support a one or two-dimensional array of modules. The number of THA modules **300** mounted to the carrier frame **800** is user selectable, and may be based, for example, on the number of wells to be processed, the number of different liquids to be dispensed, etc. The carrier frame **800** need not be fully populated.

In block **2104**, the user installs the carrier frame **800** into the dispensing instrument **2006**. The user may physically latch the carrier frame **800** into the instrument **2006** or the instrument **2006** may automatically position and latch the carrier frame **800**.

In block **2106**, the contact pads **104** of the modules **300** are electrically connected to the dispensing instrument **2006** via spring-loaded pins **2002**. The dispensing instrument **2006** provides power and control signals to the printhead **106** via the electrical connections. In some embodiments, only a single module **300** at a time is electrically connected to the dispensing instrument **2006**. In some embodiments, multiple modules **300** are individually/simultaneously connected to the dispensing instrument **2006**. In such embodiments, the dispense controller **2004** can cause multiple modules **300** to dispense the same or different volumes of liquid in parallel.

In block **2108**, the dispensing instrument **2006** electrically verifies some or all of the THAs on carrier frame **800**. Electrical verification involves ensuring that the printhead is of the correct type and that it is electrically functional.

In block **2110** liquid is added to the reservoir **112** of one or more THA modules **300** mounted on the frame **800**. In various embodiments, liquid may be added to the reservoir **112** before or after the carrier frame **800** is coupled to a dispensing instrument **2006**. Different liquids may be loaded into different reservoirs **112**, and different volumes of liquid may be added to different reservoirs **112**. Reservoirs may be loaded at any time before the module **300** is used, including immediately prior to use. Liquid can be added to the reservoirs **112** manually or automatically and in serial or parallel fashion.

In block **2112**, the dispensing instrument **2006** provides electrical signals that cause the modules **300** to discharge different numbers of droplets (e.g., pico-liter droplets) from printheads **106** of the modules **300**. The different numbers of droplets form different concentrations of the liquid in the different containers **1604** (e.g., wells of a microplate) positioned beneath the carrier frame **800**. Because some embodiments of the printhead **106** are capable of discharging a pico-liter droplet, serial dilution is not needed to provide a desired concentration of the liquid in the container **1604**.

In block **2114**, droplets discharged by the module **300** are detected using light scattering drop detection. A light source **1112** produces a light beam **1114** that propagates in a channel **1104** formed in the bottom surface of the module **300**. The channel **1104** allows the light beam **1114** to pass closer to the printhead **106** that would be otherwise possible. The light beam **1114** is scattered as a droplet is discharged from the printhead **106** and passes through the beam **1114**. The scattered light **1108** travels through a channel **1110** in the bottom surface of the module **300** to a light detector. The channel **1110** is provided at an angle of 5-25 degrees from the light beam **1114**. The light detector provides the scattered light **1108** to a droplet detection system.

In block **2116**, the dispensing instrument determines whether a desired number of droplets has been discharged. If the desired number of droplets has not been discharged, the dispensing instrument provides electrical signals that cause the modules to continue to discharge droplets. If the desired number of droplets has been discharged, the dispensing system stops droplet dispensing and performs the next operation.

The above discussion is meant to be illustrative of the principles and various embodiments of the present invention. Numerous variations and modifications will become apparent to those skilled in the art once the above disclosure is fully appreciated. It is intended that the following claims be interpreted to embrace all such variations and modifications.

What is claimed is:

1. A liquid dispensing device comprising:

a carrier frame to retain a plurality of titration head assembly (THA) modules; and

at least two THA modules, each THA module comprising;

a titration head assembly comprising:

an array of liquid droplet dispensers for dispensing individual liquid droplets;

a corresponding array of electrical connections for driving said array of liquid droplet dispensers with a dispensing instrument separate from said THA module; and

a reservoir on said THA module for receiving a supply of liquid and providing that liquid to said array of liquid droplet dispensers for dispensing; and

a frame to support each titration head assembly, wherein the frame comprises:

a plurality of lateral edges;

an opening through which the individual liquid droplets pass; and

an inlet channel formed in a bottom surface of said frame that extends from one lateral edge of said frame to said opening in said frame and an outlet channel that extends from the opening in the frame to another lateral edge of the frame, wherein the inlet channel and outlet channel are perpendicular to the opening in the frame;

a light source;

at least one light collector, wherein as the individual liquid droplets pass the inlet and outlet channels the droplet scatters light from the light source which is collected by the light collector via the inlet and outlet channels in the frame;

said carrier frame comprising at least two places, each place being configured to support one of said at least two THA modules, each place comprising an opening through which said supported one of said at least two THA modules can dispense corresponding liquid droplets to containers positioned beneath the carrier frame.

2. The device of claim **1**, wherein said carrier frame is rigid such that said carrier frame supports said at least two THA modules as said device, including said carrier frame and said at least two THA modules, is installed into a dispensing instrument.

3. The device of claim **2**, wherein said frame further comprises a handle feature with a grip area with a handle feature having a different geometry than a remainder of a frame perimeter.

4. The device of claim 1, wherein said at least two THA modules are releasably received and supported on said carrier frame and electrical contacts for connecting said THA modules to the dispensing instrument are disposed on surface opposite a dispensing port.

5. The device of claim 1, wherein said openings in the frame are aligned with industry standard microplate well spacing.

6. The device of claim 5, wherein said openings in said frames are spaced by an integer multiple of 2.25 mm to align with said industry standard microplate well spacing.

7. The device of claim 1, wherein said carrier frame is sized to support at least eight THA modules.

8. The device of claim 1, wherein said carrier frame is sized to support up to eight THA modules.

9. The device of claim 1 wherein a number frames are stackable.

10. The device of claim 1 wherein said frame further comprises machine readable identification marks.

11. The device of claim 1, wherein said at least two THA modules include different reservoirs to hold different volumes of fluid.

12. The device of claim 1, wherein a bottom surface of said frame is less than 2 millimeters below said array of liquid droplet dispensers.

13. A titration system comprising the device of claim 1:

wherein said dispensing instrument is for providing electrical signals via said electrical connections to drive said array of liquid droplet dispensers to dispense droplets of at least two different liquids, each of said at least two THA modules dispensing a different liquid, such that different concentrations of one of the two liquids in the other are dispensed by said liquid droplet dispensers into separate containers positioned beneath said carrier frame.

14. The system of claim 13, wherein said dispensing instrument is configured to hold fluid in a pico-liter range to produce said different concentrations of liquid in said separate containers without using subsequent dilution of contents of any said separate container.

15. The system of claim 13, wherein said each of said at least two THA modules comprises a flexible substrate for supporting said array of liquid droplet dispensers, electric connections and containers.

16. The system of claim 13, wherein said electrical connections comprise exposed pads for making an electrical connection with a spring-loaded pin of said dispensing instrument.

17. The system of claim 13, wherein said at least two THA modules snap into said carrier frame using a retention feature of the carrier frame that cooperatively engages an associated retention feature of said at least two THA modules.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 9,433,939 B2
APPLICATION NO. : 12/870546
DATED : September 6, 2016
INVENTOR(S) : Christie Dudenhoefer et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Column 9, Line 4, in Claim 4, delete "on" and insert -- on a --, therefor.

Signed and Sealed this
Seventeenth Day of January, 2017

Michelle K. Lee

Michelle K. Lee
Director of the United States Patent and Trademark Office